

Effect of tracheostomy timing on outcomes in patients with traumatic brain injury

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ABSTRACT

Tracheostomy following severe traumatic brain injury (TBI) is common, yet the outcomes associated with tracheostomy timing are unclear. The objective of this study was to assess hospital outcomes of tracheostomy timing in TBI patients. We retrospectively analyzed data from the National Inpatient Sample database of adult patients aged \geq 18 years with a primary diagnosis of TBI. Indexed hospitalizations of TBI patients who underwent either percutaneous or surgical tracheostomy between 1995 and 2015 in the United States were included. The interventional groups were 1) early tracheostomy (\leq 7 days) vs standard tracheostomy (\approx -14 days), vs late tracheostomy (\approx 15 days), and 2) tracheostomy vs no tracheostomy. Propensity score matching and conditional logistic regression models were used to analyze in-hospital mortality, length of hospitalization, and in-hospital complications among TBI patients in relation to tracheostomy timing. The risk of in-hospital mortality was 35% lower in patients who underwent tracheostomy vs those who did not (odds ratio 0.65; P<0.001). Patients who underwent early tracheostomy had a higher risk of in-hospital mortality compared to standard tracheostomy (odds ratio 1.69; P<0.001) or late tracheostomy (odds ratio 1.80; P<0.001). An early tracheostomy was associated with a shorter mean hospital length of stay (27 days) compared to standard (36 days) or late tracheostomy (48 days).

KEYWORDS adults; early tracheostomy; late tracheostomy; traumatic brain injury

ata on the ideal timing and associated benefits of early tracheostomy in the intensive care unit (ICU) for neurological injuries is scarce and currently unknown. Two recent meta-analyses reported a reduction in mechanical ventilation duration and ICU length of stay with early tracheostomy. However, conflicting results were noted on the risk of short- and long-term mortality among early and late tracheostomy patients with brain injuries. Likewise, meta-analyses involving a mixed critical care population have shown similar conflicting results. Previous findings are further complicated by the

variable definitions of "early" and "late" tracheostomy in the literature, with some studies defining tracheostomy within 3 and 10 days and >7 to 10 days from initiation of mechanical ventilation as early and late, respectively. Nonetheless, studies specifically looking at patients with severe head injuries have demonstrated that early tracheostomy may result in lower mortality and reduced ICU length of stay. These studies, however, are limited by varying study design and/or small sample size. Hence, the effects of tracheostomy timing on the health outcomes of patients in neurotrauma is yet to be elucidated. Our study analyzed 20 years of data

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in the National Inpatient Sample (NIS) database to identify the impact of tracheostomy timing on hospital outcomes in adult patients admitted with traumatic brain injury (TBI). We hypothesized that early tracheostomy (ET), defined as ≤ 7 days, would result in lower in-hospital mortality, a shorter duration of hospital stay, and fewer tracheostomy-related complications compared to standard tracheostomy (ST), defined as 8 to 14 days, and late tracheostomy (LT), defined as ≥ 15 days.

METHODS

We analyzed the largest inpatient care database in the United States, the NIS, to conduct a retrospective population-based study in a cohort of TBI patients who had undergone a tracheostomy procedure. The University of Texas (UTHealth) Research Ethics Board approved this study as exempt and waived the requirement of informed consent.

Demographic information including age, sex, and race were extracted. Tracheostomy-related in-hospital complications, such as tracheal stenosis (519.02) and infection of tracheostomy site (519.01), were recorded. Timing data were unavailable for the aforementioned complications with respect to tracheostomy. The Charlson Comorbidity Index (CCI)¹³ was calculated based on ICD-9-CM codes and categorized into four comorbidity groups: none, 0; mild, 1-2; moderate, 3-4; and severe, ≥ 5 . Furthermore, the Abbreviated Injury Scale (AIS), which is an anatomical-based coding system that describes a traumatic injury based on injury type, location, and severity, 14 was generated based on ICD-9-CM codes and categorized into three groups: mild, 1 or 2; moderate, 3; and severe, 4 or 5. In this study, TBI patients with a AIS head score of 6 were excluded, as they were likely deemed nonsurvivable on admission.

We analyzed the NIS database from 1995 to 2015 for all adult patients (aged \geq 18 years) with a primary diagnosis of TBI. We queried the NIS database for patients diagnosed with trauma-associated codes: intracranial injury (854), intracranial injury with skull fracture (800, 801, 803, 804), extradural hemorrhage following injury (852.4-852.5), subarachnoid hemorrhage following injury (852.0-852.1), subdural hemorrhage following injury (852.2-852.3), and cerebral laceration or contusion (851.0-851.9). Patients with a tracheostomy record (31.74, 31.1, and 31.29) were identified and stratified based on the day of tracheostomy placement from date of hospitalization. For the purpose of our study, ET was defined as <7 days; ST, as 8 to 14 days; and LT, as ≥15 days from admission. Patients receiving a tracheostomy at day 0 and 1 from admission date constituted 1.7% of the tracheostomy population and were not excluded from our cohort. The probability of a type I error due to the inclusion of these patients was negligible (<5%). Furthermore, TBI patients with tracheostomy were subdivided into craniotomy (01.2, 01.24) and/or craniectomy (01.2, 01.25). Patients who had a craniectomy and/or craniotomy following their tracheostomy were excluded because the procedure in such patients would likely have been related not to their

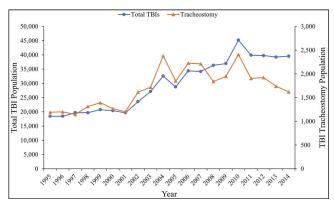


Figure 1. Incidence of traumatic brain injury (TBIs) and TBI-related tracheostomies performed between 1995 and 2014 across the United States as obtained from the National Inpatient Sample Database.

index neurological injury, but rather to other complications such as stroke or extraventricular brain hemorrhage.

Our TBI patient cohort was divided into the following groups: (1) tracheostomy vs no tracheostomy; (2) ET vs ST; (3) ET vs LT; and (4) ST vs LT. The primary outcome was the risk of in-hospital mortality among the aforementioned groups. Secondary outcomes included length of hospital stay and the risk of tracheostomy-related hospital complications, such as tracheal stenosis (519.02) and infection of tracheostomy site (519.01).

Data were presented as frequencies (percentages) for categorical variables and as mean (± standard deviation [SD]) for continuous variables. The Mann-Whitney U test and Kruskal-Wallis test were used to test mean difference in continuous variables, while a chi-square test was used to assess associations among categorical variables. To minimize the probability of selection bias, one-to-one propensity-score matching (PSM) was used to match patients within our study groups. Matching factors included demographic characteristics (age, gender, race), comorbidities (CCI), and TBI severity (craniotomy and/or craniectomy procedure, AIS head). Following PSM, conditional logistic regression models, adjusted for AIS from other body regions (face, chest, abdomen, extremities [including pelvis], and external injuries), were incorporated to assess the effects of tracheostomy and tracheotomy timing on the primary and secondary outcomes.

We conducted a subgroup analysis using ≤ 7 days as ET cutoff timing, which has been described in previous literature. Similar to our main analysis, a PSM and subsequent adjusted conditional logistic regressions were utilized to explore the relationships between these subgroups with respect to our primary and secondary outcomes. All data extraction, preparation, and analysis were conducted using RStudio (Boston, MA) and STATA 16 (College Station, TX).

RESULTS

Figure 1 depicts the incidence of total TBIs and tracheostomies following TBIs in the NIS database between 1995 and 2014 across the United States. Since 2001, the number

of TBIs and tracheostomies has gradually increased concurrently and it peaked in 2010, with a reported 45,179 cases of TBIs and 2,406 tracheostomies. Table 1 shows the unmatched baseline characteristics of TBI patients who received a tracheostomy vs those who did not. There were 624,587 hospitalized TBI patients between 1995 to 2015 in the NIS database. Of these, 35,180 (5.6%) received a tracheostomy during hospitalization and 589,407 (94.4%) did not. Compared with the nontracheostomy group, patients who received a tracheostomy were significantly younger (mean age 46.5 vs 58.2 years) and were more likely to be between 18 and 49 years old (57.8% vs 37.5%), men (75.4% vs 62.8%), and with a lower comorbidity burden (CCI 0, 70.1% vs 62.3%). The frequency of a craniectomy or craniotomy among the tracheostomy and nontracheostomy groups was similar (1.4% vs 1.5%) after excluding patients (n = 876) who underwent craniectomy and/or craniotomy after a tracheostomy. After PSM, matched pairs of 35,171 tracheostomy and nontracheostomy patients were identified (Supplementary Table S1).

Table 2 shows the unmatched baseline characteristics of TBI patients according to tracheostomy timing. Tracheostomy timing data were available for 18,051 (out of 35,180) patients. Compared to ST and LT, most patients who received ET were 18 to 49 years old (ET = 66.8%, ST = 56.2%, LT = 48.5%) and did not have comorbidities (ET = 76.8% vs ST = 66.2% vs LT = 62.9%). After PSM, we identified the following patient pairs: ET vs LT (3,052), ST vs ET (8,034), and LT vs ST (6,965). Supplementary Table S2 shows the patient characteristics for the ET, ST, and LT groups following PSM.

Figure 2 depicts the incidence of in-hospital mortality of TBI patients who did and did not undergo tracheostomy between 1995 and 2014. In the unmatched cohort, the overall rate of in-hospital mortality was higher in TBI patients who did not receive a tracheostomy compared to those who did (10.1% vs 8.8%; P < 0.001). Although 7-day in-hospital mortality was significantly higher in the nontracheostomy group (8.1% vs 1.6%), mortality after 7 days of hospitalization was significantly higher in the tracheostomy group (P < 0.001). Also, the overall in-hospital mortality rate among TBI patients who underwent ET or ST or LT was 10.7% vs 8.3% vs 10.0%, respectively. The majority of TBI patients who died following ET died within 14 days of hospitalization (68.2%), while the opposite was true (deaths after 14 days) among the ST (81.9%) and LT (99.8%) groups (Tables 1 and 2).

Table 3 depicts the adjusted in-hospital mortality among the matched groups. The risk of in-hospital mortality was significantly lower in patients who underwent tracheostomy vs those who did not (odds ratio [OR] 0.65, 95% CI 0.63–0.68, P < 0.001). Furthermore, compared to TBI patients who underwent ST or LT, ET was associated with a significantly higher risk of mortality (ET vs ST: OR 1.69, 95% CI 1.49–1.91, P < 0.001; and ET vs LT: OR 1.80,

95% CI 1.51–2.13, P < 0.001). Finally, no significant differences in mortality were noted between the ST and LT groups (P = 0.34).

Table 3 demonstrates the risk of tracheostomy-related complications among the tracheostomy timing matched groups. The risk of tracheal stenosis and infection of tracheostomy site was nonsignificant between groups. The mean length of hospitalization was calculated among the PSM groups after excluding TBI patients who had died during hospitalization (Supplementary Tables S1 and S2). TBI patients who underwent a tracheostomy spent on average 33.2 days hospitalized compared to 9.6 days in the nontracheostomy group. Moreover, ET was associated with a shorter duration of mean hospital length of stay (approximately 28 days) compared to ST (36.2 days) or LT (48.5 days).

Table 4 illustrates the risk of our primary and secondary outcomes for ET (\le 7 days) vs LT (>7 days) groups. TBI patients who had undergone an ET \le 7 days (OR 1.58, 95% CI 1.40–1.78, P<0.001) had a higher likelihood of in-hospital mortality compared to late tracheostomy >7 days. No significant differences were noted for tracheal stenosis and infection of tracheostomy site among TBI patients who had undergone an ET \le 7 days (*Table 4*).

DISCUSSION

A poor neurological state following severe TBI may require airway management due to an attenuated or loss of the pharyngeal protection reflex, excessive secretions, ventilator dyssynchrony, and/or ventilator dependence. In these patients, tracheostomy can be integral in providing airway protection and increase the chance of mechanical ventilator weaning. In our prematched sample of 624,587 TBI-related hospitalizations, 35,180 (5.6%) patients who underwent a tracheostomy were mostly young men without comorbidities and presented with higher rates of pulmonary insufficiency following trauma, which would suggest a greater degree of severe TBI in this group. Tracheostomy following TBI was associated with approximately a 35% lower risk of in-hospital mortality compared to no tracheostomy. This is congruent with another large retrospective study showing increased survival with tracheostomy following severe TBI (Glasgow Coma Scale [GCS] ≤ 8). Accurately predicting the timing of tracheostomy placement in TBI patients secondary to prolonged mechanical ventilation is challenging, though some studies have shown lower mortality, shorter ICU/hospital length of stay, and fewer complications with ET.^{3,7,16}

Due to disparities in definitions of ET in the literature, the unknown severity and pathological location of TBI, and variable concomitant injuries, caution should be exercised in comparing our findings with previously published literature. Nevertheless, previous studies have shown conflicting results in short- and long-term mortality following ET vs LT in patients with severe head injuries. ^{1,3,7,12} A meta-analysis by Dunham et al found that severe TBI patients who underwent an ET (day 3–5 post-injury) had a significantly higher risk of

Table 1. Unmatched baseline characteristics of TBI patients undergoing tracheostomy or no tracheostomy between 1995 and 2015 in the United States

Variables	Tracheostomy ($n = 35,180; 5.6\%$)	No tracheostomy (n = $589,407; 94.4\%$)	P value
Age, mean (SD), (years)	46.5 ± 19.8	58.2 ± 23.0	< 0.001
Age group, (years)			
18–49	20,318 (57.8%)	220,807 (37.5%)	< 0.001
50-64	7,292 (20.7%)	100,061 (17.0%)	
65–74	3,575 (10.2%)	74,517 (12.6%)	
≥75	3,995 (11.4%)	194,022 (32.9%)	
Gender			
Male	26,532 (75.4%)	370,298 (62.8%)	< 0.001
Female	8,639 (24.6%)	218,486 (37.1%)	
Data not available	9 (0.03%)	623 (0.1%)	
Race			
White	19,718 (56.1%)	356,412 (60.5%)	< 0.001
Black	3,735 (10.6%)	45,906 (7.8%)	
Hispanic	3,186 (9.1%)	50,273 (8.5%)	
Asian	549 (1.6%)	13,327 (2.3%)	
Native American	215 (0.6%)	3,689 (0.6%)	
Other	7,777 (22.1%)	119,800 (20.3%)	
Charlson Index			
0	24,675 (70.1%)	366,963 (62.3%)	< 0.001
1–2	8,534 (24.3%)	166,640 (28.3%)	
3–4	1,552 (4.4%)	41,036 (7.0%)	
≥5	419 (1.2%)	14,768 (2.5%)	
AIS head, mean (SD)	3.39 ± 0.66	3.40 ± 0.65	< 0.001
AIS head			
1 or 2	963 (2.7%)	29,058 (4.9%)	< 0.001
3	21,736 (61.8%)	306,954 (52.1%)	
4 or 5	12,481 (35.5%)	253,395 (43.0%)	
Craniectomy or craniotomy			
Yes	502 (1.4%)	8,543 (1.5%)	0.73
No	34,678 (98.6%)	580,864 (98.6%)	
LOS, mean (SD), (days)*	32.5 ± 25.6	6.7 ± 9.1	< 0.001
LOS, median (IQR), (days)*	26 (18-39)	4 (2-8)	< 0.001
Mortality			
Total in-hospital	3,099 (8.8%)	59,742 (10.1%)	< 0.001
7 days	549 (1.6%)	47,602 (8.1%)	< 0.001
8-14 days	708 (2.0%)	8,057 (1.4%)	
14-29 days	1,014 (2.9%)	3,375 (0.6%)	
≥30 days	825 (2.4%)	699 (0.1%)	
Data not available	3 (0.009%)	9 (0.002%)	

^{*}Patients with LOS > 365 days were excluded.

AIS indicates Abbreviated Injury Scale; IQR, interquartile range; LOS, length of stay; SD, standard deviation; TBI, traumatic brain injury.

Table 2. Unmatched baseline characteristics of TBI patients undergoing early, standard, or late tracheostomy between 1995 and 2015 in the United States

Variables	ET $(n = 8,034)$	ST (n = 6,965)	LT (n = 3,052)	<i>P</i> value
Age, mean (SD), (years)	42.7 ± 18.7	47.4 ± 20.0	50.9 ± 20.9	< 0.001
Age group, (years)				
18–49	5,365 (66.8%)	3,913 (56.2%)	1,479 (48.5%)	< 0.001
50–64	1,424 (17.7%)	1,390 (20.0%)	648 (21.2%)	
65–74	638 (7.9%)	793 (11.4%)	388 (12.7%)	
≥75	607 (7.6%)	869 (12.5%)	537 (17.6%)	
Gender				
Male	6,299 (78.4%)	5,070 (72.8%)	2,259 (74.0%)	< 0.001
Female	1,733 (21.6%)	1,894 (27.2%)	793 (26.0%)	
Data not available	2 (0.02%)	1 (0.01%)	_	
Race				
White	4,506 (56.1%)	4,047 (58.1%)	1,760 (57.7%)	< 0.001
Black	889 (11.1%)	764 (11.0%)	338 (11.1%)	
Hispanic	785 (9.8%)	726 (10.4%)	375 (12.3%)	
Asian	108 (1.3%)	121 (1.7%)	80 (2.6%)	
Native American	38 (0.5%)	27 (0.4%)	19 (0.6%)	
Other	1,708 (21.3%)	1,280 (18.4%)	480 (15.7%)	
Charlson Index				
0	6,166 (76.8%)	4,613 (66.2%)	1,920 (62.9%)	< 0.001
1–2	1,546 (19.2%)	1,882 (27.0%)	881 (28.9%)	
3–4	233 (2.9%)	349 (5.0%)	182 (6.0%)	
≥5	89 (1.1%)	121 (1.7%)	69 (2.3%)	
AIS head, mean (SD)	3.38 ± 0.66	3.41 ± 0.67	3.42 ± 0.69	< 0.001
AIS head				
1 or 2	186 (2.3%)	145 (2.1%)	84 (2.8%)	< 0.001
3	5,136 (63.9%)	4,307 (61.8%)	1,796 (58.9%)	
4 or 5	2,712 (33.8%)	2,513 (36.1%)	1,172 (38.4%)	
Craniectomy or craniotomy				
Yes	150 (1.9%)	119 (1.7%)	54 (1.8%)	0.76
No	7,884 (98.1%)	6,846 (98.3%)	2,998 (98.2%)	
LOS, mean (SD) days)*	26.7 ± 22.3	35.8 ± 26.4	48.4 ± 32.7	< 0.001
LOS, median (IQR) (days)*	22 (14-32)	29 (21-41)	40 (30-55)	< 0.001
Mortality				
Total in-hospital	860 (10.7%)	578 (8.3%)	305 (10.0%)	< 0.001
7 days	304 (3.8%)	0 (0%)	0 (0%)	< 0.001
8-14 days	278 (3.5%)	109 (1.6%)	1 (0.03%)	
15-29 days	185 (2.3%)	290 (4.2%)	84 (2.8%)	
≥30 days	93 (1.2%)	178 (2.6%)	218 (7.1%)	

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Table 2. Continued					
Variables	ET (n = 8,034)	ST (n = 6,965)	LT (n = 3,052)	<i>P</i> value	
Data not available	_	1 (0.01%)	2 (0.07%)		
Tracheostomy-related complications					
Infection of tracheostomy site	32 (0.40%)	31 (0.45%)	11 (0.36%)	0.81	
Tracheal stenosis	32 (0.40%)	23 (0.33%)	10 (0.33%)	0.75	

^{*}Patients with LOS > 365 days were excluded.

AlS indicates Abbreviated Injury Scale; ET, early tracheostomy (\leq 7 days); IQR, interquartile range; LOS, length of stay; LT, late tracheostomy (\geq 15 days); SD, standard deviation; ST, standard tracheostomy (8–14 days); TBI, traumatic brain injury.

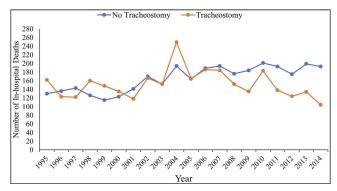


Figure 2. In-hospital mortality of patients with traumatic brain injury who did and did not undergo tracheostomy between 1995 and 2014 across the United States as obtained from the National Inpatient Sample Database.

hospital mortality compared to LT. ¹⁷ Another study noted a significant survival benefit with LT among TBI patients with a GCS \leq 8, ¹⁸ while the opposite was true in another study showing decreased mortality with ET. ⁷ Our analysis showed a lower survival benefit with ET using varying cutoff tracheostomy timing criteria. Although the underlying reasons for performing a tracheostomy in our cohort are unknown, we can reasonably presume that patients in critical condition with a high risk of mortality would not get a tracheostomy. Instead, patients with severe brain injuries who survived and needed long-term ventilation would likely undergo ET, rather than ST or LT. Clinicians may assess patients within these latter tracheostomy groups to have less severe injuries with the possibility of good neurological recovery who may be easily weaned from ventilators through standard management.

A study by Schauer et al utilized the Trauma and Injury Severity Score (TRISS) to calculate the probability of survival among their trauma patients who had undergone a tracheostomy. ¹⁹ They showed that patients with a low probability of survival were more likely to die in the ET group, while no significant differences in mortality between tracheostomy groups were noted among trauma patients with a high probability of survival. Although our analysis did not include the TRISS, we adjusted for TBI severity and concomitant injuries using the AIS and whether patients underwent a craniotomy or craniectomy; however, other important clinical factors not studied, such as absence of pupillary light reflex,

intracranial hypertension, mechanism of injury or computed tomography pathology (e.g., midline shift), may be equally important in predicting mortality. Finally, there is a high likelihood that TBI patients will survive in the ST and LT groups (vs ET) since they have already survived at least 7 days. This imparts a selection bias and thus partially explains our study findings of increased hospital mortality with ET (\leq 7 days).

TBI patients who received tracheostomy had significantly longer duration of hospital stay. Patients who do not undergo a tracheostomy are likely to be extubated or present with less severe injuries that would prompt an earlier hospital discharge. Our findings of a shorter hospital stay duration with an ET was consistent with several studies. This may either be due to a faster recovery leading to a hospital discharge or transfer to an outpatient neurological rehabilitation center. The NIS data does not provide this information.

There are several limitations to our study. The NIS database does not report GCS at admission, the mechanism of injury, type of tracheostomy performed (e.g., percutaneous vs surgical), and type of treatment received. Moreover, the lack of control of weaning and sedative/analgesics among our cohort may also affect the analysis. Due to the retrospective nature of this study, we were unable to identify a variety of disease-specific variables and match the population in each group. Despite these limitations, the present study includes a large, nationwide population sample of TBI patients who have undergone tracheostomy across a 20-year time period.

TBI patients who undergo a tracheostomy are mostly younger men with fewer comorbidities and greater injuries. In our analysis, we noted that tracheostomy following TBI, compared to no tracheostomy, was associated with a lower risk of in-hospital mortality but an increased duration of hospital stay. Moreover, when comparing tracheostomy timing (ET vs LT) following hospitalization of TBI patients, ET (≤7 days) was associated with an increased risk of in-hospital mortality and shorter duration of hospital stay, which was incongruent with our hypothesis. Various clinical factors such as TBI severity, concomitant injuries, and treatments received during hospitalization may impact these outcomes. Hence, future prospective trials should control for these confounders to assess the risk of mortality with respect to tracheostomy timing.

Table 3. Adjusted and propensity matched (1:1) analysis measuring odds ratio of in-hospital mortality and complications among TBI patients who had undergone early, standard, or late tracheostomy*

	Tracheostomy vs no tracheostomy (reference)		ET vs ST (reference)		ET vs LT (reference)		ST vs LT (reference)	
Outcomes	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
In-hospital mortality	0.65 (0.63–0.68)	< 0.001	1.69 (1.49–1.91)	< 0.001	1.80 (1.51–2.13)	< 0.001	1.09 (0.91–1.30)	0.34
Tracheostomy-related complications	S							
Infection of tracheostomy site	-	-	1.00 (0.53–1.88)	>0.99	1.28 (0.46–3.58)	0.64	2.09 (0.68–6.42)	0.20
Tracheal stenosis	-	-	1.48 (0.68–3.22)	0.32	2.28 (0.59–8.78)	0.23	1.10 (0.40–3.08)	0.85

Cl indicates confidence interval; ET, early tracheostomy (\leq 7 days); LT, late tracheostomy (\geq 15 days); OR, odds ratio; ST, standard tracheostomy (8–14 days); TBI, traumatic brain injury.

Table 4. Adjusted and propensity matched (1:1) subgroup analysis measuring odds ratio of in-hospital mortality and complications among TBI patients who had undergone tracheostomy ≤7 vs >7 days*

	Tracheostomy ≤7 vs >7 days (reference)			
Outcomes	OR (95% CI)	<i>P</i> value		
In-hospital mortality	1.58 (1.40–1.78)	< 0.001		
Tracheostomy-related complications				
Infection of tracheostomy site	1.00 (0.58–1.74)	0.99		
Tracheal stenosis	1.09 (0.59–2.00)	0.79		

Cl indicates confidence interval; OR, odds ratio; TBI, traumatic brain injury.

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